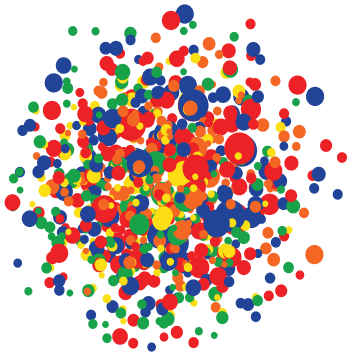

ACCURATUS
—LAB SERVICES—
THE ANTIMICROBIAL AUTHORITY

Creating Adequate Reprocessing Instructions

Help Reduce Healthcare Acquired Infections

White Paper

Adequate Reprocessing Instructions

According to the CDC "on any given day, about one in 25 hospital patients has at least one healthcare-associated infection."[1,2] Statistically, about 6-7% of all procedures/hospital visits in the U.S. result in a HAI (Healthcare Acquired/Associated Infection).[2] In other, less developed countries, the infection rate can be as high as 40%.

The six categories of HAI's are:

- Pneumonia
- Gastrointestinal illness
- Urinary Tract Infections (UTI)
- Blood Stream Infections
- Surgical Site Infections
- Other

This may lead you to question what causes these infections? The answer can sometimes be difficult to trace, but numerous studies have identified caregiver's hand hygiene as one of the major sources of infection. Catheters, central lines and surgical sites are also major sources of infection. Another player is reusable medical devices. This includes surgical equipment, dental hand pieces, nebulizers, flexible and rigid endoscopes, ultrasound probes and transducers, but also less obvious equipment such as monitors, overhead lights in a surgical suite, bed rails in a hospital room, stethoscopes, blood pressure cuffs, ventilators, and pulsometers used to test oxygen levels.[3,4]

These devices can harbor microorganisms which can spread to patients by the caregiver, by the patient touching a contaminated surface, or by the actual medical device during a procedure. In recent years, flexible duodenoscopes have been a major concern as there have been outbreaks of carbapenem-resistant Enterobacteriaceae (CRE) causing major illness and even death to patients. CRE has a 40-50% mortality rate because it has a high resistance to many, if not most available antibiotics.[5] Typically, CRE organisms are not a concern for healthy people, but patients undergoing procedures, nursing home patients, etc. are at a higher risk of contracting the organisms.[5] One example of an outbreak of CRE infections caused by duodenoscopes happened in 2015 at a UCLA hospital, where seven people become ill; with two illnesses resulting in death.[6] Two duodenoscopes were identified as the source of the outbreak at this hospital.[6] This was just one instance in a series of CRE outbreaks in the US from 2012-2015. These outbreaks caused CDC and FDA to further investigate why these kept occurring. It was discovered that the complexity in the distal end of these devices has caused them to be very difficult to adequately clean and consequently, disinfect. Duodenoscope manufacturers' cleaning procedures were updated and validated to include a more thorough cleaning process, and additionally, hospitals have now been given additional measures recommended by FDA to further reduce the risk of infection.[7] The supplemental measures for facilities and staff to consider for their facility include microbial surveillance (culturing) of the scopes, performing repeat automated endoscope reprocessor (AER) cycles, use of a liquid chemical sterilant processing system, and/or terminal sterilization utilizing Ethylene Oxide (EtO).

Outbreaks like the CRE/duodenoscope instance prove just how important it is to properly decontaminate reusable medical devices. To do so, a cleaning procedure must be performed to remove any soil that would prevent disinfection or sterilization from being effective. These soils may be blood, fat, sweat, tissue, bone fragments, bacteria, saliva, sputum, medications, lubricants, etc. If soil contaminants are not removed from surfaces, disinfection or sterilization cannot be effective as these processes may not be able to penetrate soils to ultimately reach and destroy bacterial loads. Medical device manufacturers are responsible for providing instructions for use (IFU's) of devices to the healthcare users, and these instructions must provide sufficient direction to reprocess devices adequately.

According to the U.S. Food and Drug Administration (FDA), 21 Code of Federal Regulations (CFR) 801, the labeling for medical devices shall provide adequate directions for preparation for use. In March of 2015, FDA provided a guidance document titled "Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling Guidance for Industry and Food and Drug Administration Staff." This document is intended to guide device manufacturers in the complex process of writing instructions for reprocessing and for validating those instructions.

Adequate Reprocessing Instructions

For a successful validation process, the best practice is to design the device for effective cleaning and decontamination. The more complex the device, the more difficult these processes can become. Areas of complexity are lumens, seams, buttons, mated surfaces, etc.[8] Often decontamination is overlooked in the design stage, and since the reprocessing validation is one of the final steps in the project progression prior to an FDA submission, failure to consider this can lead to submission delays, or may even require a redesign of the device. If the reprocessing is taken into consideration during early design stages, it can alleviate a lot of headaches later on and even increase your time to market.

The instructions for reprocessing are the first step in preparation for reprocessing validations. FDA[8] provides Six Criteria for Reprocessing Instructions:

1. Labeling should reflect the intended use of the device.
2. Reprocessing instructions for reusable devices should advise users to thoroughly clean the device.
3. Reprocessing instructions should indicate the appropriate process for the device.
4. Reprocessing instructions should be technically feasible and include only devices and accessories that are legally marketed.
5. Reprocessing instructions should be comprehensive.
6. Reprocessing instructions should be understandable.

The general flow of reprocessing includes a pre-cleaning step, a cleaning step, followed by either disinfection or sterilization. ISO 17664 gives examples of reprocessing instructions for reusable medical devices. Important items to consider are the types of detergents, disinfectants, or sterilization processes which are appropriate for the device. Certain chemicals or temperatures can be damaging to some materials, shortening the life of the device. It is important to determine material compatibility selection, which may be done by first contacting the manufacturer of the disinfectant or cleaning agent selected.

Common cleaning agents are enzymatic detergents; however, nonenzymatic (surfactant based) detergents can also be effective cleaning agents.[11] There are also combination cleaning/disinfecting products available, where the surfactants or detergents aide in the cleaning portion and the disinfectant can kill microorganisms. It is important to note that when using a combination product, FDA still considers cleaning and disinfection to be separate steps, and expects the cleaning validation to evaluate only the cleaning steps, and the disinfection validation to evaluate only the disinfection steps. The selection of cleaning products should be something the user can easily access for purchase. For example, if the user of the device will be cleaning it in their home, instructing to clean using a detergent and/or disinfectant that can be purchased at a local drug store or convenient store is appropriate. If a device is used in a dental office, instructions should indicate use of agents readily available in the dental field.

Selection of disinfectants should be chosen based on the level of disinfection required. Devices are classified into three classifications based on the criticality of what area in the body the device will contact, and this classification will determine the level of decontamination necessary. The classifications defined by Spaulding are described as Critical, Semicritical, and Noncritical items.[9]

Critical Items: are defined as devices that enter any sterile body cavity. Examples are surgical instruments, cardiac and urinary catheters, and implants.

Semicritical Items: are defined as devices that enter mucosal membranes or nonintact skin. An example is a flexible endoscope such as a colonoscope.

Noncritical Items: are defined as devices or equipment that may contact intact skin, but not mucous membranes. Examples are blood pressure cuffs, stethoscopes, and computers.

In addition to the criticality of the device, FDA also has a classification for devices to help determine what regulatory class the device falls under. FDA provides instructions for how to determine classification here.

Adequate Reprocessing Instructions

According to the CDC, the following levels of decontamination are required:

> **Critical Items:** sterilization
>
> **Semicritical Items:** when in contact with mucosal membranes, minimally high-level disinfection; when a device that may contact nonintact skin for a brief period or blood may contact the device, intermediate-level disinfection.
>
> **Noncritical Items:** low-level disinfection.

CDC recognizes four levels of decontamination: Sterilization, high-level disinfection, intermediate-level disinfection, and low-level disinfection. Sterilization is a process used to make a product free from viable microorganisms.[10] In a validation test, total kill of at least 6-logs (≥1 million cells) of the most resistant organism (bacterial endospores) to the sterilization process is required. The most common methods used in hospitals are steam and ethylene oxide (EO). But others, such as hydrogen peroxide sterilizers, ozone, and dry heat are also used.[10] Moist heat is the most desirable method to use due to the cycle time and no known exposure issues for users or patients. Some devices may not be capable of being sterilized using steam sterilization due to the inability to be exposed to such high temperatures. Cycle parameters should be listed in the IFU, and it is best to select a common cycle used by most healthcare facilities. For example, a common steam cycle is a pre-vacuum cycle at 132°C (270°F), with a 4 minute exposure time, and a dry time.

High-level disinfection (HLD) is the process used to kill all microorganisms, but not necessarily all endospores (bacterial spores). In a validation test, a 6-log reduction of a Mycobacterium species is required. This process uses liquids which are FDA cleared products. Click here for a list of FDA cleared high-level disinfectants. These are typically used for flexible endoscopes, but other devices can also require this level of disinfection. Most HLD's require full immersion and specific temperatures, times and rinsing methods as described on their label. This rinsing step is imperative because any residuals of disinfectant remaining on the surface of the device can be toxic to patients.

Intermediate-level disinfection is the process used to "kill viruses, mycobacteria, fungi, and vegetative bacteria, but not necessarily bacterial spores."[10] This level of disinfection is performed on devices that are commonly contacted by healthcare workers that have handled bodily fluids. Blood may come into contact with the devices; therefore, infectious disease causing organisms could contaminate the device. The surfaces need to be disinfected so that the next patient does not get infected from cross contamination. Testing is performed using four vegetative organisms and a Mycobacterium species. Some devices, for example, blood glucose meters, may also require testing against a virus or viruses in addition to bacterial organisms.

Low-level disinfection is the process used to "kill vegetative bacteria, some fungi and lipid viruses. It cannot reliably kill mycobacteria or bacterial spores."[10] Since devices that require this level of disinfection are noncritical items, there is very low risk of cross contamination; however, the surfaces do need to be decontaminated because they could become contaminated with blood-borne pathogens. Testing is performed using four vegetative organisms.

The type of water to be used for cleaning, rinsing, and final rinsing after disinfection needs to be considered and listed in the IFU. AAMI TIR34 titled "Water for the reprocessing of medical devices" lists the types of water recommended based on the intended use of the device and for each step in the process. The wrong selection of water can contribute to device malfunction, endotoxin contamination, and/or ineffective cleaning/disinfection/sterilization.[12] One key aspect for rinsing semicritical and critical devices is to reduce endotoxin. Endotoxin is a component of certain Gram-negative bacterial cell walls that can induce fever and other effects when introduced into the body. Water used to rinse devices which contact locations in the patient that can cause endotoxin reactions should be critical water, which is defined as "water that is extensively treated (usually by a multistep treatment process that could include a carbon bed, softening, DI, and RO or distillation) to ensure that the microorganisms and the inorganic and organic material are removed from the water, a final submicron filtration could also be part of the treatment process."[10]

Adequate Reprocessing Instructions

The key is to remove the endotoxin before steam sterilization, as even dead organisms can produce endotoxin; thus, the actual cells need to be removed. Cleaning procedures will typically use tap water to perform the washing step; however, some manufacturers choose to use critical water in all cleaning steps (which may be due to materials compatibility). The final rinse for cleaning should be based on the next process the device will go through. If a device will be then high-level disinfected, a tap water rinse should be sufficient. But if the device is to be sterilized in a vapor process or steam sterilizer, the final rinse should be performed using critical water as these processes do not remove any remaining dead cells.

Any brushes (size and type of bristles), wipers/cloths, syringes, tubing, attachments, bins, temperatures, etc. should be listed in the IFU to inform the user to properly perform the process.[11] Clear direction for how to protect the device from any water ingress should also be given. "The instructions should also provide sufficient detail so that the user can purchase the correct items, including any custom cleaning accessories, or identify a source for the purchase of such items."[8]

Once the instructions have been prepared, validation testing can begin. Manufacturer's should select an appropriate sample size, meaning the number of controls and replicates necessary to add statistical significance to the validation. Currently it is recommended that a minimum of three replicates be performed,[10] but this is only a minimum, and often times more replicates are performed to support the evaluation of reprocessing instructions.

FDA's guidance document and AAMI TIR3011 provide the most helpful information regarding cleaning validations. Some items to consider in a cleaning validation are:

1. Test soil
2. Dry times of the soils
3. Test markers (using validated assay methods)
4. Inoculation sites
5. Simulated use conditions
6. Worst-case processing (using minimum processing conditions)
7. Visual inspection methods

For disinfection or sterilization, some items to consider for validation testing are:

1. Test organism
2. Inorganic and organic soils
3. Disinfection/Sterilization method
4. Sterilization packaging

The keys to a successful reprocessing validation are to have a well-designed device, and an understandable, user friendly, and appropriate IFU for reprocessing. Providing an IFU to the end user where they can properly perform the cleaning and disinfection or sterilization will help ensure patient safety.

It is hard to imagine going in for a routine colonoscopy and contracting a deadly infection because the cleaning instructions were not adequate. With the HAI rate being on average 6-7% of all procedures, any additional measures to reduce this rate are monumental as patient's lives are at the mercy of healthcare workers and the medical devices being utilized. In the end, a better reprocessing procedure equals a safer device.

Adequate Reprocessing Instructions

References:

1. Center for Disease Control, Healthcare-associated Infections, April 24, 2017. https://www.cdc.gov/winnablebattles/healthcareassociatedinfections/index.html
2. Center for Disease Control, HAI Data and Statistics, October 25, 2016. https://www.cdc.gov/hai/surveillance/index.html
3. Otter, JA., Yezli, S., and GL French. The role played by contaminated surfaces in the transmission of nosocomial pathogens. Infection Control Hosp Epidemiol, 2011 July, 32(7):687-99. https://www.ncbi.nlm.nih.gov/pubmed/21666400
4. O'Flaherty, N., and L. Fenelon. The stethoscope and healthcare-associated infection: a snake in the grass or innocent bystander? J. Hosp Infect., 2015 Sep. 91(1):1-7. https://www.ncbi.nlm.nih.gov/pubmed/26092471
5. Center for Disease Control, Carbapenem-resistant Enterobacteriaceae in Healthcare Setting, March 1, 2016. https://www.cdc.gov/hai/organisms/cre/index.html
6. Martinez, M., Lah, Kyung, and Traci Tumura, CNN. UCLA hospital cites medical scopes in superbug CRE outbreak. February 20, 2015. http://www.cnn.com/2015/02/19/healthcaliforniahospital-deadly-bacteria-superbug-cases/index.html
7. FDA. Supplemental Measures to Enhance Duodenoscope Reprocessing: FDA Safety Communication. August 4, 2015. https://www.fda.gov/medicaldevices/safety/alertsandnotices/ucm454766.htm
8. Guidance for Industry and FDA Staff - Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling. U.S. FDA March 17, 2015.
9. Rutala, William A., Weber, David J., and the Healthcare Infection Control Practices Advisory Committee (HICPAC). Guideline for Disinfection and Sterilization in Healthcare Facilities, 2008 (Updated February 15, 2017). https://www.cdc.gov/infectioncontrol/pdf/guidelines/disinfection-guidelines.pdf
10. Designing, testing and labeling reusable medical devices for reprocessing in health care facilities: A guide for device manufacturers. AAMI TIR12:2010.
11. A compendium of processes, materials, test methods, and acceptance criteria for cleaning reusable medical devices. AAMI TIR30:2011.
12. Water for reprocessing of medical devices. AAMI TIR34: 2014.

About Accuratus Lab Services

Accuratus Lab Services is the trusted partner and industry leader to the developers, manufacturers, and the users of antimicrobials and has been for over 25 years. We provide our clients with the most comprehensive range of microbiology, virology, and product chemistry services to support product development, claims, regulatory registration, and end-user validations of antimicrobial products used in most industries. Accuratus Labs is continuously expanding capabilities to serve the antimicrobial, medical device, pharmaceutical, paints and coatings, treated fabrics, cosmetic and personal care industries and more.

Our client-focused scientific, quality assurance, technical staff has built an unparalleled reputation for technical expertise, regulatory compliance knowledge, and superior client service. Our scientific data is of the highest quality, and our reports have earned the distinguished record of acceptance with regulatory agencies in the United States, Canada, and abroad.

Accuratus Lab Services
1285 Corporate Center Drive, Suite 110
Eagan, MN 55121
Phone: (877) 287-8378
info@accuratuslabs.com

ACCURATUS
—LAB SERVICES—
THE ANTIMICROBIAL AUTHORITY

10-13ARIWP-092017-1